UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/393,066	02/23/1995	JOHN H. WOLFE	PENN-0065	1030

7590 02/20/2008

LICATA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053

EXAMINER	
CROUCH, DEBORAH	
ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
02/20/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte JOHN H. WOLFE and NIGEL W. FRASER

Appeal 2007-2964
Application 08/393,066
Technology Center 1600

Decided: February 19, 2008

Before TONI R. SCHEINER, ERIC B. GRIMES, and RICHARD M. LEBOVITZ, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method of expressing DNA *in vivo* in central nervous system (CNS) cells, which the Examiner has rejected as nonenabled. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

BACKGROUND

"The pluripotent hematopoietic stem cell is a major target for either replacement by transplanted normal allogeneic cells or correction by gene transfer in disorders such as lysosomal storage diseases. . . . However, bone

marrow transplantation has not been very effective in delivering enzyme to the CNS, which is affected in most lysosomal storage diseases." (Spec. 3.)

One "approach to delivering gene products to the CNS is using neurotropic viruses as vectors to transfer the gene into CNS cells" (*id.* at 5). "Infection with herpes simplex virus (HSV-1), a neurotropic virus, begins with viral replication in epithelial tissues. After initial replication at the site of infection, HSV-1 establishes latent infection in the nervous system." (*Id.*) "The transcripts made during latency have been called latency-associated transcripts (LATs). . . . [I]t has been thought that the promoter of the LAT gene could be used to express foreign genes during latency." (*Id.* at 6.)

The Specification discloses a method of "delivering foreign genes to the central nervous system (CNS) of a mammal by administering to a mammal a recombinant neurotropic virus capable of expressing the foreign gene in the CNS of the mammal" (Spec. 1). The Specification provides working examples that describe construction of an HSV-1-based vector encoding a β-glucuronidase (GUSB) gene under the control of the LAT promoter (*id.* at 20-23) and administration of the vector to "Adult MPS VII mice" (*id.* at 25). The Specification states that GUSB activity was detected in the brains and trigeminal ganglia of the treated mice "up to 126 days (greater then 4 months)" after infection (*id.*)

DISCUSSION

1. CLAIMS

Claims 1 and 3-9 are pending and on appeal. Claim 1 is representative and reads as follows:

1. A method of stably expressing a selected DNA sequence in the central nervous system of a mammal comprising administering to peripheral

neuron cells of a mammal a neurotropic viral vector which infects cells of the central nervous system of the mammal, said vector containing a selected DNA sequence operatively linked to a LAT promoter so that said selected DNA sequence is stably expressed for at least four months by infected central nervous system cells.

2. ENABLEMENT

Claims 1 and 3-9 stand rejected under 35 U.S.C. § 112, first paragraph, as nonenabled, on the basis that the only use for the claimed method is in gene therapy, and therefore the claimed method must provide a therapeutic effect in order to be enabled. (Answer 4: "While the claimed invention requires only stable expression of the selected DNA sequence, the specification provides no use for mere stable expression. . . . The specification does not disclose a use for the claimed method of delivery absent a treatment or therapeutic effect.")

The Examiner finds that "[a]t the time of filing, gene therapy was not developed sufficiently that the mere showing of delivery of a gene to a particular tissue would have been viewed as enabling gene therapy" (*id.*). The Examiner cited several references as support for her position that gene therapy faced technical obstacles at the time the instant application was filed

(*id.* at 5)[1] and that "the use of HSV-1 vectors in gene therapy protocols was unpredictable" (*id.* at 5-6).

The Examiner acknowledges the Specification's working examples, but finds that they do not provide the required guidance because "the mice, which are models for mucopolysaccharidosis VII due to mutations in their GUSB gene, are not described as showing any alleviation of symptoms associated with the disorder due to the treatment" (*id.* at 7). The Examiner concludes that

> as the specification provides no guidance over than that provided by the art, and the art's clear comments that gene therapy . . . was enabled [sic, not enabled?] at the time of filing, to implement the presently claimed invention would require the skilled artisan to engage in an undue amount of experimentation without a predictable degree of success.

(*Id.* at 8.)

Appellants argue that the claims are not directed to "methods for treating a disease of the CNS, rather the subject matter of the instant claims relates to methods for stably expressing a selected DNA sequence in the central nervous system" (Appeal Br. 11). Appellants argue that the Specification discloses how to make the vector recited in the claims and how

[1] The Examiner cites Fink et al., "Advances in the development of herpes simplex virus-based gene transfer vectors for the nervous system," Clinical Neuroscience, Vol. 3, pp. 284-291 (1996); Blomer et al., "Applications of gene therapy to the CNS," Human Molecular Genetics, Vol. 5, pp. 1397-1404 (1996); Eck et al., "Gene-based therapy," in *Goodman & Gilman's The Pharmacological Basis of Therapeutics*, 9th edition, pp. 77-101, McGraw-Hill (1996); and Wolfe et al., "Herpesvirus vector gene transfer and expression of β-glucuronidase in the central nervous system of MPS VII mice," Nature Genetics, Vol. 1, pp. 379-382 (1992).

to administer it to peripheral neuron cells so that it is expressed for at least four months (*id.*).

Appellants also argue that "demonstration of therapeutic benefit is **not** a requirement of patentability" (*id.* at 12). Appellants submitted a declaration under 37 C.F.R. § 1.132 by Laura M. Plunkett as evidence "that data provided in the instant specification are demonstrative of a pharmacological effect . . . and thus, therapeutic utility," which they argue is the appropriate standard for enablement (*id.* at 13).

We agree with Appellants that the Examiner has applied an overly stringent standard for enablement in this case. "[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993). "That *some* experimentation may be required is not fatal; the issue is whether the amount of experimentation required is 'undue.'" *In re Vaeck*, 947 F.2d 488, 495 (Fed. Cir. 1991) (emphasis in original). Some experimentation, even a considerable amount, is not "undue" if, for example, the specification provides a reasonable amount of guidance as to the direction in which the experimentation should proceed. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

The enablement analysis must be focused on the product or method defined by the claims. "Title 35 does not require that a patent disclosure enable one of ordinary skill in the art to make and use a perfected, commercially viable embodiment absent a claim limitation to that effect." *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1338 (Fed. Cir. 2003).

See also In re Cortright, 165 F.3d 1353, 1359 (Fed. Cir. 1999) (claims to method of "restoring hair growth" encompassed achieving full head of hair but did not require it).

The claims on appeal are directed to a method of stably expressing a particular gene in mammalian CNS, not a method treating a disease via gene therapy. It is true that the Specification contemplates the use of the claimed method in gene therapy but practicing the claimed method does not require a therapeutically effective result.

The Examiner's apparent position that the Specification cannot teach how to use the claimed method unless it teaches solutions to all the problems in the field of gene therapy is contrary to controlling case law. *See, e.g., In re Brana*, 51 F.3d 1560, 1568 (Fed. Cir. 1995).

In *Brana*, the claims were directed to compounds disclosed as anti-cancer agents. *Id.* at 1562. The USPTO rejected the claims as nonenabled, *id.* at 1563-64, despite working examples in Brana's specification showing treatment of cancer in a mouse model. *Id.* at 1562-63. The USPTO argued that the results of the mouse testing "are not reasonably predictive of the success of the claimed compounds for treating cancer in humans." *Id.* at 1567. The court concluded that this position "confuses the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption." *Id.* The *Brana* court held that "[u]sefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an

invention in this field becomes useful is well before it is ready to be administered to humans."

Similarly here, the claims are directed to a method of stably expressing a gene in mammalian CNS cells, and Appellants' Specification provides a working example of stable expression for more than four months in the CNS of a mouse model. The Examiner has interpreted the claims as being directed to a method of treating disease via gene therapy, and has discounted the Specification's working example because it does not describe the treated mice as "showing any alleviation of symptoms" (Answer 7). However, enablement – especially in the context of pharmaceutical inventions – includes an expectation of further research and development. In the pharmaceutical field, an invention can be enabled well before it is ready to be administered to humans. Thus, enablement is not precluded even if the claims encompass methods, such as gene therapy, that have not yet overcome all the obstacles to their clinical use.

In summary, the Examiner has not adequately shown that undue experimentation would have been required to practice the *claimed* method; specifically, achieving stable expression of a selected gene in mammalian CNS cells by introducing the gene, under the control of the LAT promoter, in a neurotropic vector to peripheral neuron cells of the mammal. The claims do not require therapeutically effective treatment of any disease, and the Examiner erred in concluding that such an effect was required to satisfy 35 U.S.C. § 112, first paragraph. We therefore reverse the rejection for nonenablement.

REVERSED

saj

LICATA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053